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A histomorphometric evaluation of heparin-induced bone loss after discontinuation of heparin treatment in rats.

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Although it is well established that long-term heparin therapy causes osteoporosis, it is unknown whether heparin-induced bone loss is reversible when heparin treatment is stopped. To address this question, we randomized rats to once daily subcutaneous injections of either unfractionated heparin (1.0 U/g or 0.5 U/g) or saline for 28 days and then followed the rats for an additional 28 days off treatment. Based on histomorphometric analysis of the distal third of the right femur proximal to the epiphyseal growth plate, 1.0 U/g heparin caused a 30% loss in cancellous bone volume over the first 28 days. This was accompanied by a 137% increase in osteoclast surface and a 60% decrease in both osteoblast and osteoid surface. One month after cessation of heparin treatment, no recovery in these parameters was observed. Similarly, serum levels of alkaline phosphatase, a biochemical marker of bone formation, which continued to decrease over the course of heparin treatment, showed no signs of recovery in the subsequent 28 days off treatment. To explore the mechanism responsible for the prolonged effect of heparin on bone, we repeated the experiment giving 125I-labeled heparin in place of unlabeled heparin. 125I-labeled heparin was found to accumulate in bone during the course of its administration, and be retained in bone for at least 56 days after stopping heparin treatment. These findings suggest that heparin-induced osteoporosis is not rapidly reversible because heparin is sequestered in bone for an extended period.

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